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BAFF levels in patients with ankylosing spondylitis and response to anti-tumor necrosis factor treatment

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The serum levels of B cell-activating factor of the TNF family (BAFF), also called B lymphocyte stimulator (BLyS), have been shown to be increased in patients with several inflammatory rheumatic diseases [1-3]. Although B cells are not commonly associated with the pathogenesis of ankylosing spondylitis (AS), some findings corroborate their potential involvement. Dense infiltrations of B cells were found in the spine of patients with active inflammation [4]. Moreover, anti-tumour necrosis factor treatment (aTNF)-naïve patients showed a good treatment response to B cell depletion with rituximab [5]. As BAFF is a potent B cell survival and maturation factor, we analyzed BAFF levels in AS patients before and after aTNF. The study protocol has been approved by the Institutional Review Board of the Canton of Zurich.

Serum samples were obtained from 49 patients with definite AS, as well as from 35 healthy controls (HC), after written informed consent. aTNF with adalimumab (n=15) or infliximab (n=20) was initiated in 35 patients with Bath AS Disease Activity Index (BASDAI) levels > 4, according to the decision of the treating rheumatologist. Serum was obtained again 3 months later in these subjects. Treatment response was defined as a 50% relative decrease in BASDAI or an absolute decrease in 2 BASDAI points on a scale 0-10. BAFF serum levels were measured using a commercially available ELISA (R&D systems, Minneapolis, Minnesota, USA).

Baseline (BL) serum BAFF levels were lower in AS patients compared to HC (median 1.1 ng/ml [5th-95th percentile: 1-1.9] vs. 1.5 ng/ml [5th-95th percentile: 0.8-2.0] respectively; $p=0.002$). Only in 3/49 AS patients BAFF levels exceeded slightly the upper cutoff limit of 2.1 ng/ml (corresponding to the mean +2SD of the levels in HC). BL BAFF levels did not correlate with BASDAI, CRP, HLA-B27 positivity, disease duration or co-medication with DMARDs. The median BAFF levels increased modestly 3 months after initiation of aTNF (BAFF3mo), from 1.06 ng/ml to 1.38 ng/ml (Wilcoxon paired sign rank test 95% confidence interval (CI) of increase: +0.09;+0.39; $p=0.003$) and nearly reached levels observed in HC. The increase was observed in patients responding to aTNF as well as in non-responders (0.26 ng/ml [95% CI 0.09-0.46] vs. 0.18 ng/ml [95% CI -0.1-0.52]). After stepwise variable selection of a multiple regression model for BAFF3mo as a function of BL BAFF and the other variables mentioned above, we found that BAFF3mo was 1.32-fold higher in HLA-B27 positive patients and was positively related to BL CRP (overall p -value of model <0.002, adjusted $R^2=0.43$).

As a conclusion, BAFF is not elevated in AS patients, in contrast to other chronic inflammatory rheumatic diseases [2,3]. Therapeutic inhibition of the BAFF pathway with belimumab [6] or atacicept [7] is therefore not warranted in AS. As opposed to patients with rheumatoid arthritis showing a decrease in BAFF levels following a good response to TNF inhibition [8], we observed a slight increase in BAFF after aTNF. Whether this finding might explain the fact that B cell depletion with rituximab is not very effective following aTNF in AS remains unclear.

Figures

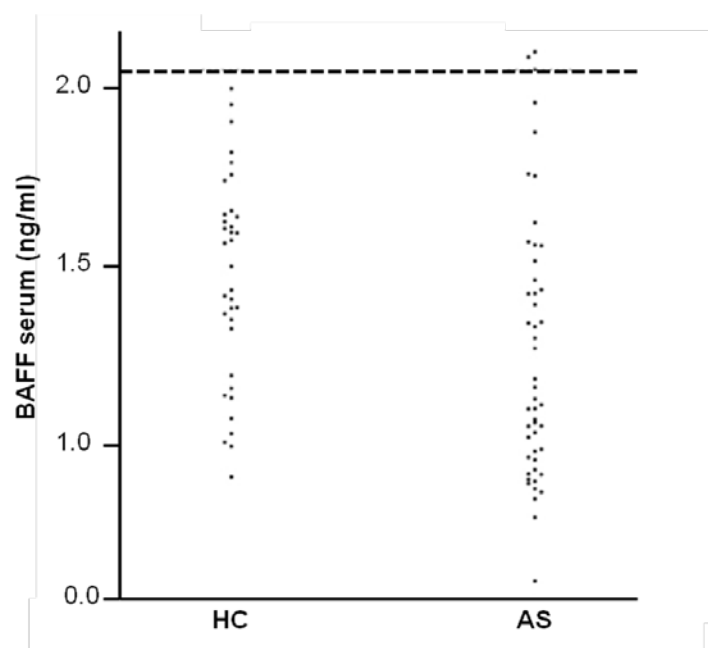


Fig. 1. Serum levels of BAFF (ng/ml) in individual patients with ankylosing spondylitis (AS) compared to healthy controls (HC). The broken line indicates the cut-off (defined as mean +2SD of levels in HC).

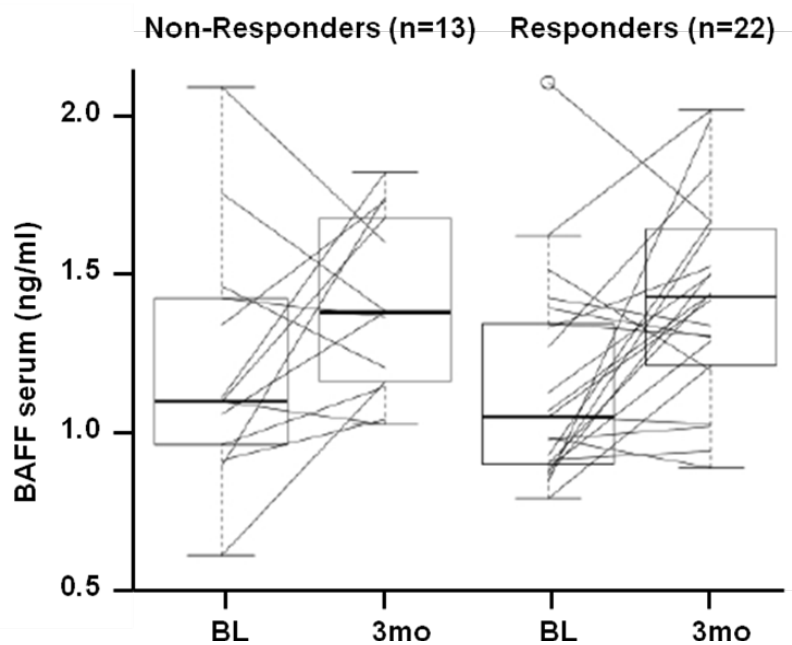


Fig. 2. Effect of TNF inhibitor treatment on BAFF serum levels in treatment responders vs. non-responders. Serum samples were collected at baseline (BL) and 3 months treatment initiation.

Disclosure of interest

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